Antibody design using LSTM based deep generative model from phage display library for affinity maturation

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Abstract

Molecular evolution is an important step in the development of therapeutic antibodies. However, the current method of affinity maturation is overly costly and labor-intensive because of the repetitive mutation experiments needed to adequately explore sequence space. Here, we employed a long short term memory network (LSTM)—a widely used deep generative model—based sequence generation and prioritization procedure to efficiently discover antibody sequences with higher affinity. We applied our method to the affinity maturation of antibodies against kynurenine, which is a metabolite related to the niacin synthesis pathway. Kynurenine binding sequences were enriched through phage display panning using a kynurenine-binding oriented human synthetic Fab library. We defined binding antibodies using a sequence repertoire from the NGS data to train the LSTM model. We confirmed that likelihood of generated sequences from a trained LSTM correlated well with binding affinity. The affinity of generated sequences are over 1800-fold higher than that of the parental clone. Moreover, compared to frequency based screening using the same dataset, our machine learning approach generated sequences with greater affinity.